Alpha BioCom
Precision Integrity Passion
10th Anniversary

MONTHLY
Vol. 1 No. 7
www.alphabiocom.com

Autumn has Fallen

Summer's over, but our yearlong celebration continues

Autumn is now in full swing. That's sad for those of us who love the sun and sandy beaches that summer offers, but, as William Shakespeare was quick to remind us, "summer's lease hath all too short a date."

Now it's time once again for raking leaves, digging out your sweaters from the back of the clothes closet, hockey season, Halloween decorating, and seeing what the latest "pumpkin-flavored" fad will be (pumpkin walnut crunch bagel, anyone? Or perhaps a pumpkin spice Hershey Kiss?).

The coming of autumn also means that we're in the home stretch of AlphaBioCom's celebration of our 10th anniversary. We're happy to have you along for this yearlong ride!

The focus of this issue is on Orphan Diseases, classified as such when the disease affects fewer than 200,000 people in the United States, or if there is no expectation that the cost of developing a drug will be recovered by sales in the US. There are approximately 7,000 diseases today that are classified as rare or orphan diseases.

You can see a timeline of some of the developments in the classification of orphan drugs on this page, and check inside for a more detailed discussion of Orphan Diseases and how they've been recognized and approached. While Orphan Diseases may be rare, there are plenty of places to turn for information, such as Orpha.net (http://www.orpha.net/), which points out on its homepage that "There is no disease so rare that it does not deserve attention."

Since you read this newsletter thoroughly, every month, we know you know what comes next, right? This is where we once again invite you to check out the new and improved AlphaBioCom website (www.AlphaBioCom.com) and feel free to leave comments and suggestions about our newsletter and our organization. We can be found on Twitter at @alphabiocom, and you can connect with us on LinkedIn.

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A LOOK AT ORPHAN DRUGS

More than 1600 orphan drugs were approved by the US Food and Drug Administration from 2005–2014. Below is a list of just a small fraction of the drugs that have been approved to help in the treatment of Orphan Diseases.

2015: 159 drugs were designated as Orphan Disease drugs by the FDA
- (S)-7-(1-(9H-purin-6-ylamino)ethyl)-6-(3- fluorophenyl)-3-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one was designated for treatment of Hodgkin lymphoma (Incyte Corporation)

2014: 268 drugs were designated as Orphan Disease drugs by the FDA
- (R)-1-(2,2-difluorobenzo [d][1,3] dioxol-5-yl)-N-(1-(2,3-dihydroxypropyl)-6-fluoro-2-(1- hydroxy-2-methylpropan-2-yl)-1H-indol-5-yl) cyclopropanecarboxamide was designated for the treatment of cystic fibrosis (Vertex Pharmaceutials Inc.)

2013: 235 drugs were designated as Orphan Disease drugs by the FDA
- 4-(6-(4-(piperazin-1-yl)phenyl_pyrazolo[1,5-a]pyrimidin-3-yl)quinoline hydrochloride was designated for treatment of Fibrodysplasia ossificans progressive (La Jolla Pharmaceutical Company, Inc.)

2012: 177 drugs were designated as Orphan Disease drugs by the FDA
- Adeno-associated virus transgene of follistatin was designated for treatment of Duchennes and Becker's muscular dystrophy (Milo Biotechnology)

2011: 186 drugs were designated as Orphan Disease drugs by the FDA
- (-)-(3aR,4S,7aR)-4-Hydroxy-4-m-tolylethynyl-octahydro-indole-1-carboxylic acid methyl ester was designated for treatment of Fragile X syndrome (Novartis Pharmaceuticals Corp)

2010: 170 drugs were designated as Orphan Disease drugs by the FDA
- Autologous CD34+ cells transfected with lentiviral vector containing the human WAS cDNA (Telethon 003) was designated for treatment of Wiskott Aldrich syndrome (GlaxoSmithKline Intellectual Property Development)

2009: 140 drugs were designated as Orphan Disease drugs by the FDA
- Dasiprotimut-T (Biovaxid) was designated for treatment of follicular lymphoma (Biovest International, Inc.)

2008: 139 drugs were designated as Orphan Disease drugs by the FDA
- 5-[(E)-2-(4-hydroxyphenyl)-ethenyl]benzene-1,3diol was designated for the treatment of MELAS syndrome

2007: 99 drugs were designated as Orphan Disease drugs by the FDA
- Centhromycin was designated for treatment of patients exposed to inhalation anthrax

2006: 123 drugs were designated as Orphan Disease drugs by the FDA
- Amikacin (Arikace) was designated for treatment of bronchopulmonary *Pseudomonas aeruginosa* infections in cystic fibrosis patients

2005: 96 drugs were designated as Orphan Disease drugs by the FDA
- 4-(3-Methanesulfonyl-phenyl)-1-propylpiperidine HCl was designated for treatment of Huntington's disease

Streams ...They're Not Just for Fishing Anymore

Online music stores, streaming audio have changed the way we listen to music

Big news in the world of music technology arrived in November 2005, when iTunes entered the US Top 10 sales list for the first time. It marked not only digital sales' entry into the top 10 forms of purchasing music, but it was the first time that a digital sales model—from which listeners could purchase while in the comfort of their own homes—bested its large, traditional brick-and-mortar competitors.

According to Russ Crupnick, then a music and movies industry analyst for The NPD Group, "it's not inconceivable to see (iTunes) cracking into higher ground in the foreseeable future."

It's probably safe to say, however, that no one could have predicted that iTunes would spark a revolution in music sales, leading to the rise of digital music stores such as CD-Baby and CDUniverse and to online retailers adding digital music to their sites (amazon.com, for example, launched its digital music store in 2007).

As a whole, digital and physical album sales declined 11 percent in 2014. Interestingly, the only format that experienced a growth was vinyl sales, which increased a whopping 52% in 2014 with 9.2 million vinyl albums sold.

That certainly isn't to say that fewer people are listening to music. It simply means that, with new technology, we continue to create new ways to enjoy music. And while sales may have declined in 2014, on-demand music streaming experienced a 54.5% increase in total streams over 2013, with 78.6 billion audio streams.

Streaming services such as Spotify, Pandora, Google Music, Apple Music, Rdio, and Songza dominate the digital landscape; some are pay services, while others offer a free, commercial-supported option as well as ad-free premium service for a fee.

Think about how you listened to music in 2005. Compact discs were plentiful and home music systems and car audio systems often featured multiple-CD changers so you could load up six CDs and listen for hours and hours without ever having to change a station or remove a disc. Now, many cars come with iPod/iPhone adapters/capabilities, satellite radio, or streaming audio, so that the driver never needs to "touch that dial."

Back in 2005, before iPods truly became ubiquitous, some of us were proud owners of MP3 pioneers such as the Rio Riot, a cassette player-sized MP3 player that held thousands of songs and allowed the user to play music by artist, album, song, or via the creation of a personalized playlist. Perhaps you still had Winamp running on your desktop so you could listen to your MP3 collection while on the computer.

Soon enough we transferred all our music onto iPods—the ones with the classic click wheel—and our music libraries expanded exponentially as 15, 30, 60, 80, and 160 GB iPods allowed for tens and hundreds of thousands of songs to be stored on a device no larger and not much thicker than a credit card.

As iPods and their competitors (anyone unlucky enough to own a Zune?) flooded the marketplace, it became easier and easier to store more and more music on smaller and smaller devices. With the ability to store digital media to the "Cloud," even the smallest device with a simple Internet connection can access unlimited music.

Access to familiar and new music (we highly suggest NoiseTrade.com and ReverbNation.com as ways to discover fantastic independent artists from around the globe) has become more widespread and easier than ever. Who knows what the next 10 years will bring in terms of music technology? But with more options more accessible than ever, it remains a great time to be a fan of music of all genres.

From left: The ill-fated Zune, Microsoft's attempt to compete with the iPod; Spotify has become one of the most popular, most complete, and best sources of streaming audio; the merger of Sirius and XM satellite radio into a single entity took place on November 12, 2008; the iPod Classic with the click wheel controller – a place to store thousands of songs and albums; nowadays, your smartphone does it all, serving as the only device you need to purchase, store, and/or stream music.

Orphan Diseases and Their Treatments

Just because a disease is 'rare,' that doesn't mean it's not important to study and treat

The Orphan Drug Act (ODA) was created in response to the dearth of development activity for diseases in which the total affected population is small and the risk/reward ratio not worth pursuing by most pharma company standards. The ODA was passed by the United States Congress in 1983 and offers incentives to induce companies to develop drugs and medical devices for individuals with rare disorders.

Drugs and biologics intended for the safe and effective treatment, diagnosis, or prevention of diseases that affect fewer than 200,000 people in the US, or that affect more than 200,000 people, but for which companies are not expected to recover the costs of development and marketing, are given orphan status by the Orphan Drug Designation program. An analogous program, the Humanitarian Use Device program designates a device that is intended to benefit patients by treating or diagnosing a disease or condition that affects fewer than 4,000 individuals in the US per year.

No single cutoff number has been agreed upon for which a disease is considered "rare." A rare disease occurs in fewer than 200,000 individuals using the US definition, or fewer than 5 per 10,000 individuals using the European Union definition. In the US, 47% of rare disorders affect fewer than 25,000 people. Examples of rare diseases include Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, Duchenne/Becker muscular dystrophy, and Castleman's Disease. With only a single diagnosed patient, ribose-5-phosphate isomerase deficiency is presently considered the rarest genetic disease. For perspective, researchers have estimated that as many as 1-in-10 Americans suffers from a rare disease. Global estimates suggest that there are between 5000 and 7000 rare diseases with more than 55 million people estimated to suffer from a rare disease in Europe and in the US.

The mission of the FDA Office of Orphan Products Development (OOPD) is to advance the evaluation and development of products (drugs, biologics, devices, or medical foods) that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. OOPD provides incentives for sponsors to develop products for rare diseases. Under the ODA, orphan drug sponsors qualify for 7-year FDA-administered market Orphan Drug Exclusivity, tax credits of up to 50% of R&D costs, R&D grants, protocol development assistance and priority review of new drug applications (a 6-month review rather than the standard 10-month review). A new drug application that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication for another disease that is not considered an orphan disease.

Similar incentives are available from the EU, including a 10-year marketing exclusivity. The FDA and EMA (European Medicines Agency) have aligned their regulations such that The Common EMEA/FDA Application for Orphan Medicinal Product Designation can be used when filing with both organizations.

The granting of an orphan designation request does not alter the standard regulatory requirements and process for obtaining marketing approval. As with the development of other agents, safety and efficacy must be established through adequate and well-controlled trials.

The ODA has been widely recognized as a success. Before Congress enacted the ODA in 1983, only 38 drugs were approved in the US specifically to treat orphan diseases. Between January 1983 and June 2004, some 1129 different orphan drug designations were granted by the OOPD and 249 orphan drugs received marketing authorization. In contrast, the decade prior to 1983 saw fewer than 10 such products gain approval. From the passage of the ODA in 1983 until May 2010, the FDA approved 353 orphan drugs and granted orphan designations to 2116 compounds. There are more than 400 orphan designated drugs in clinical development.

Even with the large number of approvals over the last few years, treatments exist for only about 10 percent of these pathologies. The proportion of FDA approvals for orphan drugs has been increasing though, and now accounts for about one-third of all approvals. In 2014, 15 of the 35 new drugs approved by the FDA had received orphan drug designation, the greatest number since the ODA was passed. The market size has also mushroomed, with the 2013 market for orphan drugs worth an estimated US$90 billion. Global forecasts for sales of orphan drugs are predicted to be more than US$176 billion by 2020.

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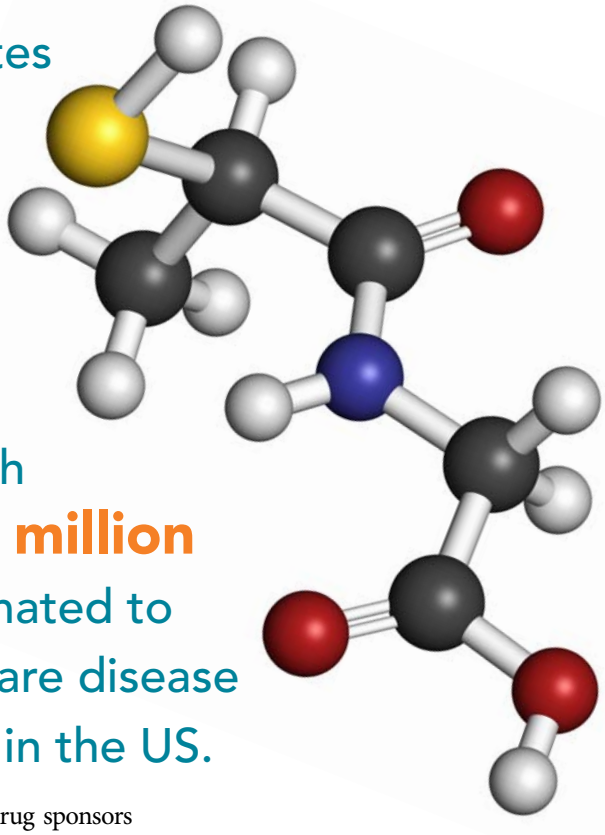

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Providing Children with Hands-on Experiences

The Science Education Academy Inc. (SEA), is a local STEM nonprofit whose aim is to support elementary grade students (grades 2–5) in their science education with hands-on exposure and experience with scientific method and inquiry while strengthening their observation, logic, and communication skills. This program was established in 2008 as a partnership between the Science Education Academy Inc., the White Rock Baptist Church Ministry to Youth and Children, and the EE Just Biomedical Society at the University of Pennsylvania. This program was targeted to a group of low-income students from a variety of schools in West Philadelphia.

I have been involved with the organization since it began in 2008. I started by volunteering as a teacher on Saturday mornings. In addition, as a member of the Executive Board for the EE Just Biomedical Society, I spearheaded the volunteer recruitment effort from within the EE Just organization. During subsequent years, as the SEA program expanded from teaching children in grades 2–3 to teaching grades 2–5 and mentoring students for the George Washington Carver Science Fair, my recruitment efforts expanded to other student organizations within the University of Pennsylvania, and in the last couple of years to include students from Drexel and Jefferson universities.

AlphaBioCom Editorial Assistant Carolina Pombo (third from left) and fellow volunteers at a Science Education Academy event.

For three years, I have also been a member of the SEA organizing committee, involved in organizing the Parent Orientation Day, scheduling volunteers, teaching on Saturday mornings and planning for the SEA academic year, and revising the curriculum to teach students grade- and age-appropriate topics that reinforce the city's public school curriculum. I have also been involved in organizing supplementary programs throughout the year. These have included a Women in Science lunch, Philly to Lesotho Exchange, summer field trips (Johnson Pond [University of Pennsylvania] and the NBC weather station) and presentations by the Academy of Natural Sciences, NBC, and local musicians, as well as a cow heart dissection with the collaboration of a local city physician.

As a member of the organizing committee, I am also involved in planning for the annual SEA Community Science carnival that takes place in the summer and includes experiments for children 6 to 12 years old and workshops for their parents.

For more information, email SEA or visit the SEA webpage or the Facebook page.

MEET THE STAFF

Tara Martin, *Account and Project Director*

As AlphaBioCom's Account and Project Director, Tara is responsible for developing and maintaining relationships with clients through a strong commitment to success, passion, precision, and integrity. She manages internal teams to ensure quality standards and deadlines are met; and helps to ensure the accuracy, consistency, and regulatory compliance of all materials.

Tara graduated from the University of Rhode Island with a bachelor's degree in Human Counseling and Family Studies. She has spent time as a Sales Representative for Johnson & Johnson Vistakon and as an Adult Vaccines Sales Representative, Product Manager (for Cervarix), Senior Product Manager, and Marketing Director with GlaxoSmithKline, where she earned numerous awards for her efforts in customer retention, tactical plan development, and consumer marketing.

Tara started at AlphaBioCom in January 2011.

Liqing Xiao, PhD, *Scientific Communications Manager*

As a Scientific Communications Manager, Liqing works with the scientific lead and assists with development of abstracts, posters, slide decks, and both primary data and review manuscripts.

Liqing earned a Bachelor's Degree in Biochemistry at Nanjing University, and received her PhD in Biochemistry and Molecular Biology at the Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences. She served a Postdoctoral Fellowship at the University of Pennsylvania, School of Medicine, where she received a training award in prostate cancer research from Department of Defense.

She was a research associate at the Children's Hospital of Pennsylvania, and served a Fellowship at the Center for Technology Transfer, University of Pennsylvania. Liqing has co-authored several manuscripts published in peer-reviewed scientific journals.

Liqing spent more than a year as a Clinical Writer for ECRI Institute before coming to AlphaBioCom in June 2015.